EXHIBIT 1

Biotechnology and Chemical Pharmaceutical Customer Partnership Meeting
Wednesday, June 13, 2007

United States Patent and Trademark Office
Madison Auditorium North
600 Dulany Street, Alexandria, Virginia

The most recent quarterly meeting for the Biotechnology and Chemical Pharmaceutical Customer Partnership was held on March 7, 2007 at the U.S. Patent and Trademark Office. The Biotechnology and Chemical Pharmaceutical Customer Partnership is designed and developed to be a forum to share ideas, experiences, and insights between individual users and the USPTO. The USPTO does not intend to use these customer partnership groups to arrive at any consensus. Invitations to participate will indicate that individual opinions are sought, rather than a group consensus and that the meetings are intended to be informal in nature and have varying participants. These customer partnership groups are formed with full recognition of the USPTO's responsibility under the Federal Advisory Committee Act (FACA), and that these customer partnership groups are not established as FACA compliant committees.

This meeting is also available on-line. Participation is limited to the first 200 individual registrants; so, if you are interested in attending this meeting, please click on the link below to register:

On-Line
Registration

We value our customers in obtaining feedback from individual participants is important in our efforts to continuously improve the quality of our products and services. Your willing participation is helpful in providing us with insights and experiences in this informal process to assist us.

The next meeting of the U.S. Patent and Trademark Office Biotechnology and Chemical Pharmaceutical Customer Partnership is scheduled for Tuesday, June 13, 2007 from 9:00 am to 4:30 pm at Auditorium North in Madison Building, 600 Dulany Street, Alexandria, Virginia.

For information of future meetings and presentations, please go to http://www.cabic.com/bcp/.

Please contact Cecilia Tsang at 571-272-0562, or by fax at 571-273-0562, or email Cecilia.Tsang@uspto.gov to decline or confirm your attendance by June 7, 2007.

Morning Session

9:00-9:20	Greetings and Overview	John LeGuyader, Bruce Kisliuk, Christopher Low, Directors, Technology Center 1600
9:20-10:00	Peer Review Pilot	Jack Harvey, Director, TC2100
		Andy Faile, Director,

10:00-10:40	Suite of Products	TC2600
10:40-10:55	Break	
10:55-12:00	Restriction Between Product and Process Inventions	Bruce Campell, Supervisory Patent Examiner, Art Unit 1648

12:00-1:15 Lunch

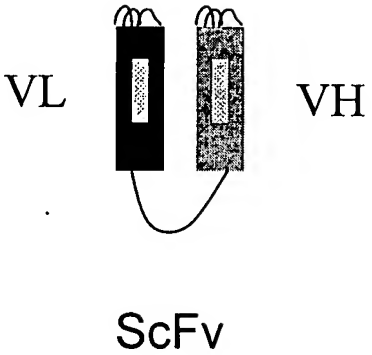
Afternoon Session

1:15-2:00	Enablement Issues in the Examination of Antibody	Larry Helms, Supervisory Patent Examiner, Art Unit 1643
2:00-2:45	RNAI Patent Space	James Schultz, Supervisory Patent Examiner, Art Unit 1635
2:45-3:00	Break	
3:00-3:45	Guidance on Routine Optimization	Jean Wiz and Dave Nguyen, tQASs, TC1600
3:45-4:00	Closing Remarks/Discussion	John LeGuyader, Bruce Kisliuk, Christopher Low, Directors, Technology Center 1600

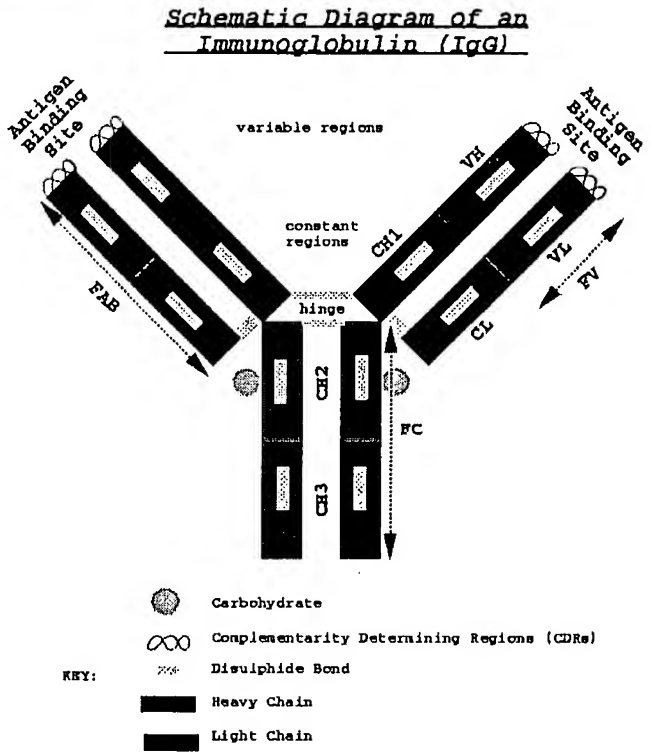
Enablement Issues in the Examination of Antibodies

Larry R. Helms
SPE, AU 1643
Technology Center 1600
USPTO
(571) 272-0832
Larry.helms@uspto.gov

Antibody Structure

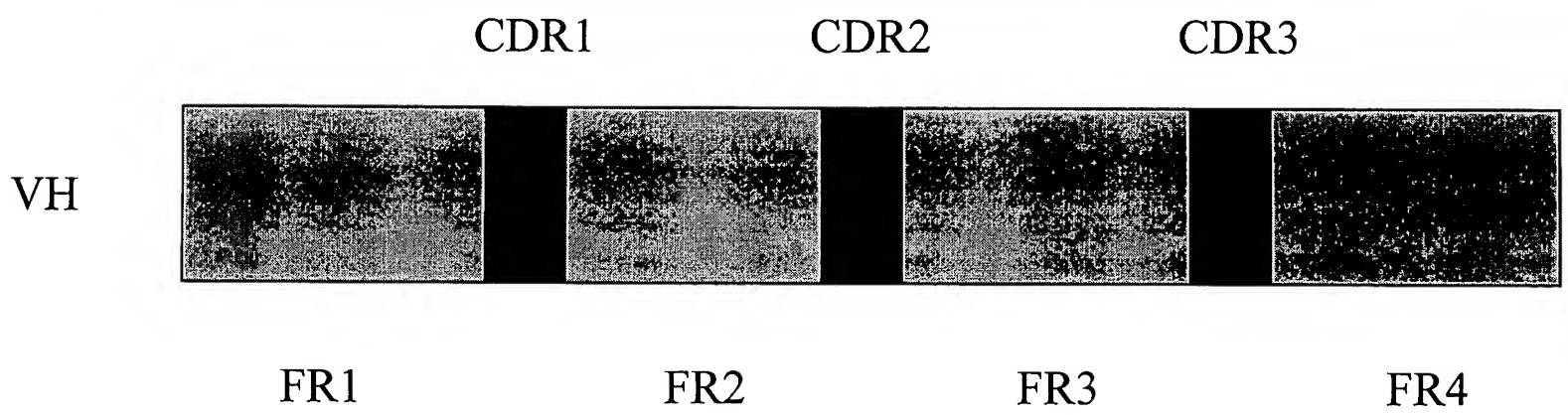


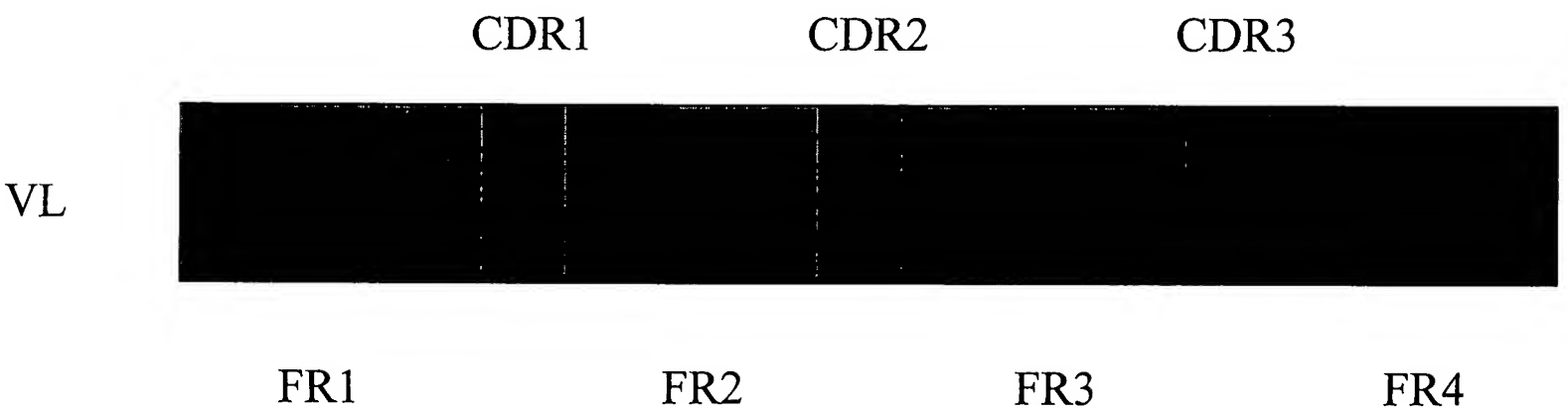
ScFv



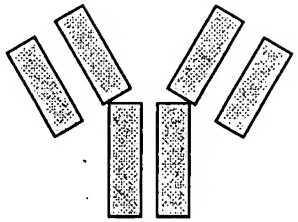
Adapted from people.cryst.bbk.ac.uk/~ubcg07s/gifs/igG.gif

Variable domain of Antibodies

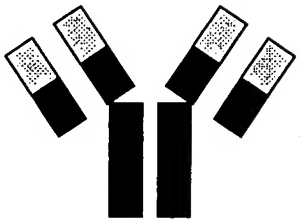




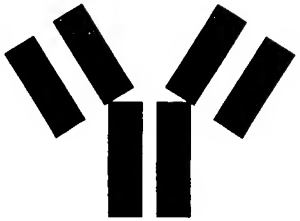
Humanization of Antibodies



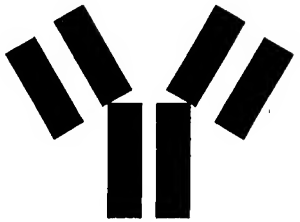
Mouse



Chimaeric



Humanized



Human

Enablement

35 USC § 112

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

MPEP 2164.01(a) Undue Experimentation Factors (*In re Wands*):

(1) The breadth of the claims

(2) The nature of the invention

(3) The state of the prior art

(4) The level of one of ordinary skill

(5) The level of predictability in the art

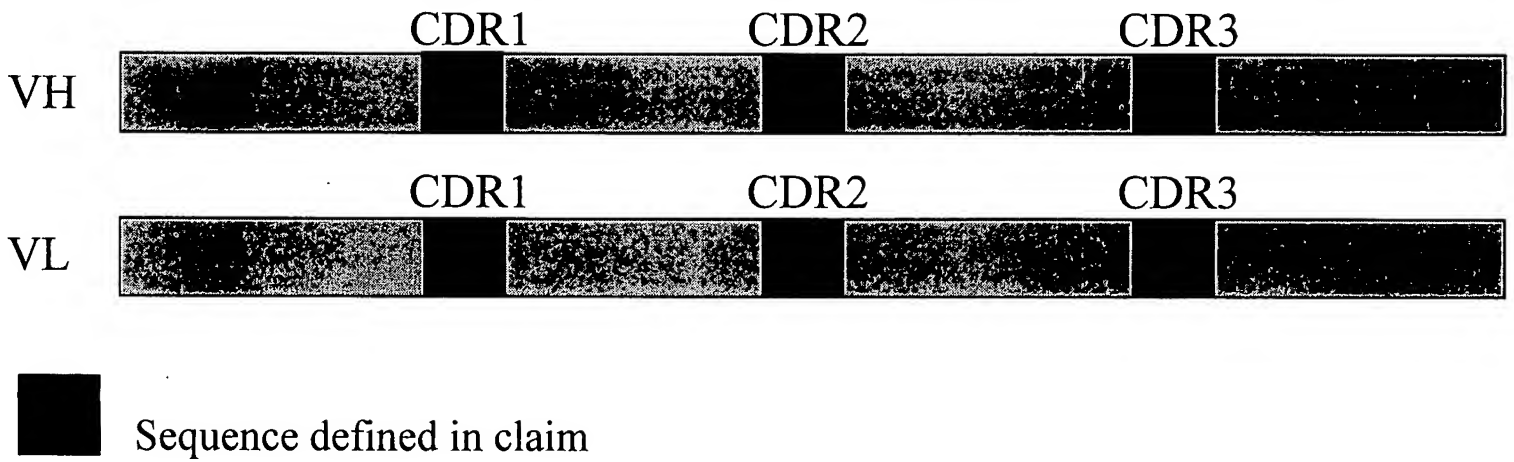
(6) The amount of direction provided by the inventor

(7) The existence of working examples

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Example 1

- Claim: An isolated antibody that binds to human antigen X, said antibody comprises a heavy chain variable domain comprising the 3 CDRs in SEQ ID NO:1 and a light chain variable domain comprising the 3 CDRs in SEQ ID NO:2.



Specification

- Discloses antigen X from human tissue.
- Discloses antigen X is over-expressed in cancer tissue vs. normal tissue.
- The instant application produced an antibody that binds antigen X that contains a VH of SEQ ID NO:1 and a VL of SEQ ID NO:2, as well as explicitly disclosing humanized and chimaeric antibodies.
- The instant application provides examples of detection of cancer in human subjects with an antibody that binds antigen X.

State of the Prior Art

- It was well known at the time the application was filed that the heavy and light polypeptide chains each contribute three CDRs to the antigen binding region of the antibody molecule.
- The prior art[1] taught humanization of antibodies by transfer of the 6 CDRs from a donor framework region to an acceptor framework region and retention of antigen binding.

[1]Queen et al., PNAS (1988) 86:10029-10033,
Riechmann et al., Nature (1988) 332:323-327

Analysis

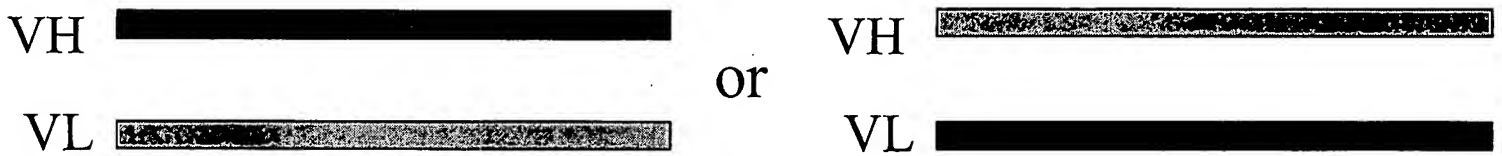
- In light of the prior art disclosing the CDRs as being the essential structure of the antibody's binding site, the identification of the specific CDR sequences in the specification provides enough structure to define the antibody's binding site.
- In addition, the prior art for humanization supports obtaining successful antigen binding by transferring the 6 CDRs from a donor framework to an acceptor framework.

Analysis (cont.)

- Thus, it would not have been undue experimentation to obtain an antibody that would bind antigen X and comprise the 6 CDRs as specifically defined in the claim at the time of filing.
- Therefore, a claim that defines an antibody that binds antigen X and comprises a heavy chain variable region comprising the 3 CDRs in SEQ ID NO:1 and a light chain variable region comprising the 3 CDRs in SEQ ID NO:2 meets the requirements under 35 U.S.C. 112, first paragraph, for enablement.

Example 2

- Claim 1. An isolated antibody that binds to human antigen X, said antibody comprises a heavy chain variable domain comprising SEQ ID NO:1.
- Claim 2. An isolated antibody that binds to human antigen X, said antibody comprises a light chain variable domain comprising SEQ ID NO:2.



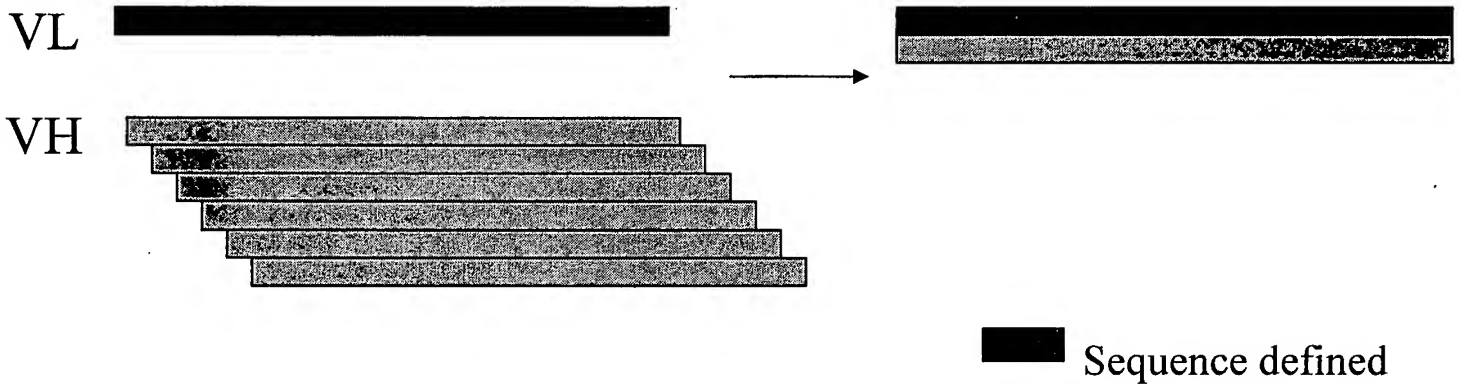
Sequence defined in claim

Specification

- Discloses antigen X from human tissue.
- Discloses antigen X is over-expressed in cancer tissue vs. normal tissue.
- The instant application produced an antibody that binds antigen X that contains a VH of SEQ ID NO:1 and a VL of SEQ ID NO:2, as well as explicitly disclosing humanized and chimaeric antibodies.
- The instant application provides examples of detection of cancer in human subjects with an antibody that binds antigen X.

State of the Prior Art

- There are several prior art[2] references that teach methods of producing antibodies that bind a specific antigen by using a specific VL (or VH) and screening a library of the complimentary variable domains.



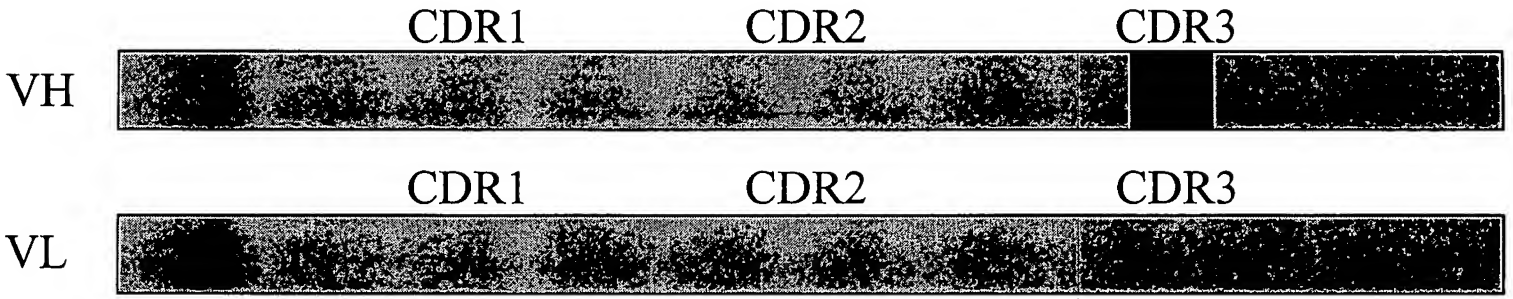
[2]Portolano et al., The Journal of Immunology (1993) 150:880-887
Clarkson et al., Nature (1991) 352:624-628

Analysis

- In light of the prior art disclosing methods of obtaining antibodies that bind an antigen by screening complementary variable domain libraries, the specification's disclosure of an antibody that binds a specific antigen comprising a defined VH or VL sequence would provide enough structure for one skilled in the art to practice the invention.
- Therefore, claims directed to an antibody that binds a specific antigen and comprises a defined VH or VL sequence meet the requirements under 35 U.S.C. 112, first paragraph, for enablement.

Example 3

- Claim: An isolated antibody that binds to human antigen X, said antibody comprises a heavy chain variable domain and a light chain variable domain, said heavy chain variable domain comprises the CDR3 in SEQ ID NO:1 (VH).



Sequence defined in claim

Specification

- Produced a series of antibodies that bind antigen X and the antibodies were not random combinations of VH and, i.e., VL they had specific VH domains paired with specific VL domains.
- The VH domains are highly homologous to each other and share not only CDR3, but also were nearly identical in framework regions (3-6/124 residues) as well as CDR1 (3/5)[1] and CDR2 (6/16)[1] regions.

| ▌ indicates region where residues differ

[1] indicates residues that are identical out of number of residues in the CDR

Specification (cont.)

- Analysis of the VL sequences of these antibodies reveals that these domains are highly homologous to each other. The framework regions are nearly identical and the VL domains are identical in CDR1 and CDR2 regions. The CDR3 (8/10)[1] regions are highly homologous to each other.
- The instant application suggests that it was well established in the art at the time the invention was made that the CDR3 region alone can determine the specificity of the antibody.

[redacted]

[1] indicates residues that are identical out of number of residues in the CDR

State of the Prior Art

- Prior art for obtaining an antibody with only CDR3 of the VH defined:

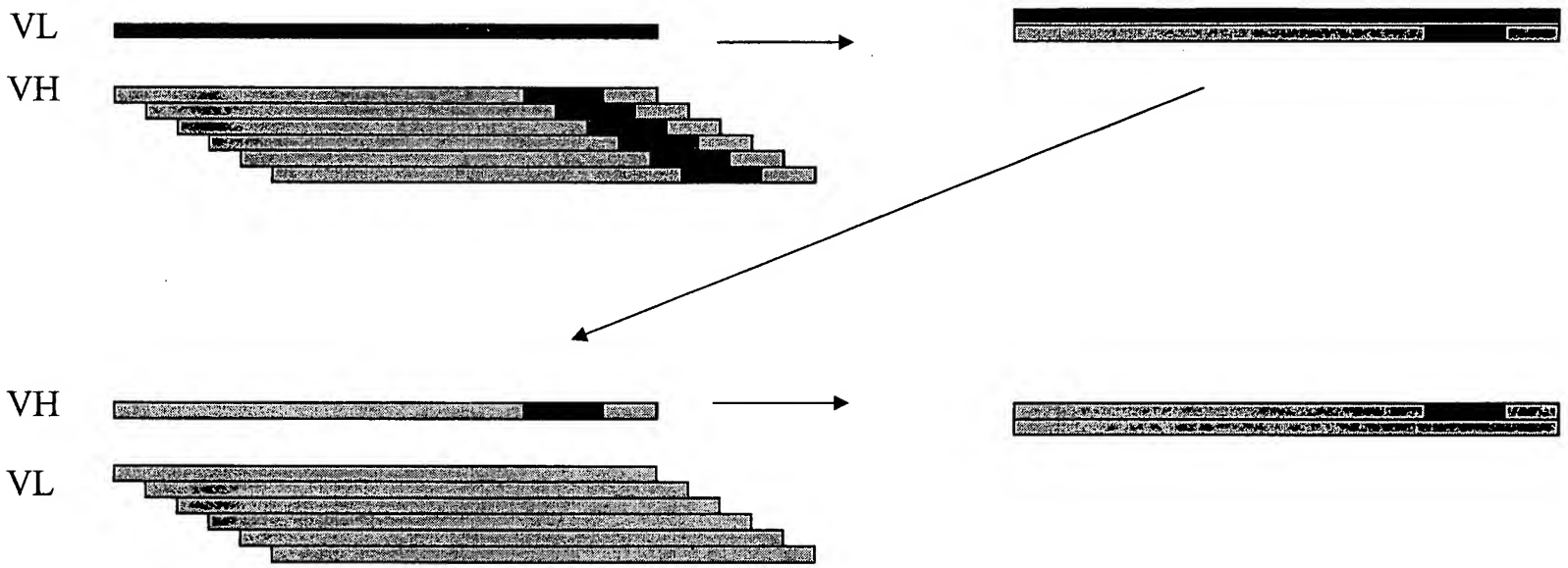
Klimka et al., British Journal of Cancer (2000) 83: 252-260: Klimka et al describe a screening process using a mouse VL and a human VH library with CDR3 and FR4 retained from the mouse VH. After obtaining antibodies, the VH was screened against a human VL library to obtain antibodies that bound antigen.

Beiboer et al., J. Mol. Biol. (2000) 296:833-849: Beiboer et al describe a screening process using the entire mouse heavy chain and a human light chain library. After obtaining antibodies, one VL was combined with a human VH library with the CDR3 of the mouse retained. Antibodies capable of binding antigen were obtained.

Rader et al., PNAS (1998) 95:8910-8915: Rader et al, describe a process similar to Beiboer et al above.

State of the Prior Art (cont.)

Method for screening



State of the Prior Art (cont.)

- The prior art methods for screening rely on a two step process where each step results in an antibody, however, each step requires one of the variable domains to be a defined sequence and the defined variable domain provides enough structure to obtain an antibody.
- The prior art methods do not result in an antibody solely by keeping CDR3 in the VH defined and randomizing the rest of the VH and VL domains.

State of the Prior Art (cont.)

- Prior art indicating the CDR3 region in the VH domain is important in antigen binding:

MacCallum et al., J. Mol. Biol. (1996) 262: 732-745: Analyzed many different antibodies for interaction with antigen and found that although CDR3 of the VH dominate the interaction, a number of residues outside the CDRs make antigen contacts and residues in the CDRs are important for backbone conformations.

Pascalis et al., the Journal of Immunology (2002) 169: 3076-3084: Grafting of CDRs onto a human framework required some residues in all 6 CDRs as well as specific frameworks.

Casset et al., BBRC (2003) 307, 198-205: Constructed a peptide mimetic of an anti-CD4 antibody binding site using 24 residues formed from residues from 5 of the CDRs. Casset et al., state that although CDR H3 is at the center of most antigen interactions, clearly other CDRs play an important role in recognition.

State of the Prior Art (cont.)

Vajdos et al., J. Mol. Biol. (2002) 320: 415-428: Antigen binding is primarily mediated by the CDRs but more highly conserved framework segments are mainly involved in supporting CDR loop conformations and, in some cases, framework residues also contact antigen.

Padlan et al., PNAS (1989) 86:5938-5942: Padlan et al describe the crystal structure of an antibody-lysozyme complex where all 6 CDRs contribute at least one residue to binding and one residue in the framework is also in contact with antigen.

Lamminmaki et al., JBC (2001) 276:36687-36694: Lamminmaki et al describe the crystal structure of an anti-estradiol antibody in complex with estradiol where, although CDRH3 plays a prominent role, all CDRs in the light chain make direct contact with antigen (even CDRL2, which is rarely directly involved in hapten binding).

State of the Prior Art (cont.)

- The prior art indicated that, in some instances, the CDR3 region is important. However, this region is not solely responsible for binding. The conformation of other CDRs, as well as framework residues influence binding.

State of the Prior Art (cont.)

- Transfer of only CDR3 in the VH and retention of antigen binding.

Barbas et al., PNAS (1995) 92: 2529-2533: Transferred the CDR3 of the VH of three anti-DNA antibody to an anti-tetanus toxoid antibody and retained DNA binding in 2/3 antibodies.

It was known in the art that antibodies that bind dsDNA can be generated by reconstruction of the CDR3 in the heavy chain of an antibody as well as transplantation of a 17 amino acid alpha-helical DNA binding domain into CDR3 of the heavy chain[3].

[3]McLane et al., PNAS (1995) 92:5214-5218,
Barbas et al., J. Am. Chem. Soc. (1994) 116:2161-2162

Analysis

- The claim is broadly drawn to any antibody that binds antigen X and comprises a heavy chain variable region comprising CDR3 in SEQ ID NO:1.
- The specification discloses antibodies with highly homologous VH and VL domains and identical VH CDR3 regions.
- The specification does not disclose that CDR3 of the VH alone can be transferred to just any framework and paired with just any VL and retain antigen binding.

Analysis (cont.)

- The specification does not provide any examples to support that CDR3 of the VH or VL is solely responsible for antigen binding.
- The prior art does not show screening for antibodies by just defining CDR3. The methods rely on using an entire VH or VL and screening random complimentary chains.
- The prior art does not show that a CDR3 is universally solely responsible for antigen binding.

Analysis (cont.)

- The prior art does not support a definition of an antibody structure solely by defining the CDR3 sequence of a VH or VL.
- Based on this analysis a claim to an isolated antibody that binds to human antigen X, said antibody comprises a heavy chain variable domain and a light chain variable domain, said heavy chain variable domain comprises the CDR3 in SEQ ID NO:1, does not meet the requirements of 35 U.S.C. 112, first paragraph, for enablement.

Questions

Larry R. Helms
SPE, AU 1643
Technology Center 1600
USPTO
(571) 272-0832
Larry.helms@uspto.gov

Yvonne (Bonnie) Eyler
Quality Assurance Specialist
Technology Center 1600
USPTO
(571) 272-0871
Yvonne.eyler@uspto.gov